PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
22339 WO-BUR		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP2004/012464	04/11/2004	04/11/2003
Applicant		
ROCHE DIAGNOSTICS GMBH		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 09 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      ☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

Patent Department (TR-E) → PE		
Case	Int.-Nr.	
Literatur erfasst: Lit.sheet ☐ Endnote ☐	Zeichen:	Datum:

4. With regard to the **title,**
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      ☐ as suggested by the applicant.
      ☐ as selected by this Authority, because the applicant failed to suggest a figure.
      ☐ as selected by this Authority, because this figure better characterizes the invention.
   b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/012464

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Article 52 (2)(d) EPC - Presentation of information

The claims were only searched with regards to the underlying method of generating a reference data base for distinguishing leukemia subtypes.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-27 (partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-27 (partially)

A method for distinguishing MLL-PTD-positive AML from other AML subtypes, the method comprising determining the expression level of the marker AAK1. Use of said marker for the manufacture of a diagnostic. A diagnostic kit containing said marker and an apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression level of AAK1.

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2. claims: 1-27 (all partially)

Inventions 2-1100

Methods for distinguishing MLL-PTD-positive AML from other AML subtypes and methods for distinguishing specific subtypes against all other subtypes and against each other, the method comprising determining individually the expression level of the markers listed in table 1.1, positions 2-50,and in tables 2-3. Use of said markers for the manufacture of diagnostics. Diagnostic kits containing said markers and apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression levels of said markers.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/012464

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/574 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), SCHNITTGER SUSANNE ET AL: "Acute Myeloid Leukemia (AML) with Partial Tandem Duplication of the MLL-Gene (MLL-PTD) Can Be Discriminated from MLL-Translocations Based on Specific Gene Expression Profiles." XP002270207 Database accession no. PREV200300335802 abstract -/--	1-27

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 March 2005	09. 06. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Thumb, W

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Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	& BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 1202, 44th Annual Meeting of the American Society of Hematology;Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971	
Y	SCHOCH CLAUDIA ET AL: "Acute myeloid leukemias with reciprocal rearrangements can be distinguished by specific gene expression profiles" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 99, no. 15, 23 July 2002 (2002-07-23), pages 10008-10013, XP002215484 ISSN: 0027-8424 the whole document in particular tables 1 and 2	1-27
Y	WO 03/039443 A (DEUTSCHES KREBSFORSCH ;HAFERLACH TORSTEN (DE); EILS ROLAND (DE); K) 15 May 2003 (2003-05-15) the whole document in particular Examples 4, 6 and 7	1-27
Y	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), HAFERLACH TORSTEN ET AL: "Gene Expression Profiling Is Able To Reproduce Different Phenotypes in AML as Defined by the FAB Classification." XP002269981 Database accession no. PREV200300357598 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 731, 44th Annual Meeting of the American Society of Hematology;Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971	1-27

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), NEBEN KAI ET AL: "Acute Myeloid Leukemia with Normal Karyotype and Mutation of the FLT3 or MLL Gene Are Characterized by Specific Gene Expression Profiles." XP002270208 Database accession no. PREV200300336869 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 2172, 44th Annual Meeting of the American Society of Hematology;Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971 -----	1-27
Y	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2001 (2001-11-16), SCHNITTGER SUSANNE ET AL: "Partial tandem duplications (PTD) of the MLL gene: A study of 1603 patients reveals high frequency in secondary acute myeloid leukemia and low association with trisomy 11" XP002270209 Database accession no. PREV200200261466 abstract & BLOOD, vol. 98, no. 11 Part 1, 16 November 2001 (2001-11-16), page 801a, 43rd Annual Meeting of the American Society of Hematology, Part 1;Orlando, Florida, USA; December 07-11, 2001 ISSN: 0006-4971 -----	1-27
Y	KOHLMANN A ET AL: "MOLECULAR CHARACTERIZATION OF ACUTE LEUKEMIAS BY USE OF MICROARRAY TECHNOLOGY" GENES, CHROMOSOMES & CANCER, XX, XX, vol. 37, no. 4, August 2003 (2003-08), pages 396-405, XP008025253 the whole document in particular table 2 -----	1-27

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2001 (2001-11-16), SCHOCH CLAUDIA ET AL: "Specific abnormalities on the genomic level result in a distinct gene expression pattern detected by oligonucleotide microarrays: An analysis of 25 patients with AML M2/t(8;21), AML M3/M3v/t(15;17), and AML M4eo/inv(16)" XP002269491 Database accession no. PREV200200129822 abstract & BLOOD, vol. 98, no. 11 Part 1, 16 November 2001 (2001-11-16), pages 92a-93a, 43rd Annual Meeting of the American Society of Hematology, Part 1;Orlando, Florida, USA; December 07-11, 2001 ISSN: 0006-4971	1-27
Y	EP 1 043 676 A (WHITEHEAD BIOMEDICAL INST) 11 October 2000 (2000-10-11) the whole document	1-27
Y	GOLUB T R ET AL: "Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 286, no. 5439, 15 October 1999 (1999-10-15), pages 531-537, XP002207658 ISSN: 0036-8075 cited in the application the whole document	1-27
Y	DUGAS M ET AL: "A comprehensive leukemia database: integration of cytogenetics, molecular genetics and microarray data with clinical information, cytomorphology and immunophenotyping" LEUKEMIA, MACMILLAN PRESS LTD, US, vol. 15, no. 12, December 2001 (2001-12), pages 1805-1810, XP002263731 ISSN: 0887-6924 the whole document	1-27

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DUGAS MARTIN ET AL: "Impact of integrating clinical and genetic information." IN SILICO BIOLOGY, vol. 2, no. 3, 2002, pages 383-391, XP001179418 ISSN: 1386-6338 (ISSN print) the whole document	1-27
A	CONNER SEAN D ET AL: "Identification of an adaptor-associated kinase, AAK1, as a regulator of clathrin-mediated endocytosis" JOURNAL OF CELL BIOLOGY, vol. 156, no. 5, 4 March 2002 (2002-03-04), pages 921-929, XP002270210 ISSN: 0021-9525 the whole document	1-27
A	ALIZADEH A ET AL: "THE LYMPHOCHIP: A SPECIALIZED CDNA MICROARRAY FOR THE GENOMIC-SCALE ANALYSIS OF GENE EXPRESSION IN NORMAL AND MALIGNANT LYMPHOCYTES" COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY, BIOLOGICAL LABORATORY, COLD SPRING HARBOR, NY, US, vol. 64, no. 1, 1999, pages 71-78, XP001099007 ISSN: 0091-7451 the whole document	1-27
A	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), KOHLMANN ALEXANDER ET AL: "A Simplified and Partially Automated Target Preparation Method for Gene Expression Profiling." XP002269495 Database accession no. PREV200300367771 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 4287, 44th Annual Meeting of the American Society of Hematology;Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971	1-27

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP2004/012464

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03039443 A	15-05-2003	EP 1308522 A1	07-05-2003
		WO 03039443 A2	15-05-2003
		EP 1470247 A2	27-10-2004
EP 1043676 A	11-10-2000	CA 2304876 A1	09-10-2000
		EP 1043676 A2	11-10-2000
		JP 2001017171 A	23-01-2001
		US 2003017481 A1	23-01-2003
		US 6647341 B1	11-11-2003
		US 2003073083 A1	17-04-2003

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
ROCHE DIAGNOSTICS GMBH
Patent Department (TR-E)
Attn. Burger, Alexander
P.O. Box 11 52
D-82372 Penzberg
GERMANY

REGISTERED MAIL

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Applicant's or agent's file reference 22339 WO-BUR	**PAYMENT DUE** within 30 ~~months~~/days from the above date of mailing
International application No. PCT/EP2004/012464	International filing date *(day/month/year)* 04/11/2004
Applicant ROCHE DIAGNOSTICS GMBH	Date of mailing *(day/month/year)* 17/03/2005

1. This International Searching Authority

(i) considers that there are 1100 *(number of)* inventions claimed in the international application covered by the claims indicated ~~below~~/on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~/on the extra sheet:

(ii) [X] has carried out a partial international search (see Annex) [ ] will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

see annex

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

EUR 1,550.00	x	1099	=	EUR 1,703,450.00
Fee per additional invention		number of additional inventions		total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. [ ] Claim(s) Nos. _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Wolfgang-Peter Schießl

Form PCT/ISA/206 (July 1992)

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/EP2004/012464

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-27 (partially)

A method for distinguishing MLL-PTD-positive AML from other AML subtypes, the method comprising determining the expression level of the marker AAK1. Use of said marker for the manufacture of a diagnostic. A diagnostic kit containing said marker and an apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression level of AAK1.

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2. claims: 1-27 (all partially)

Inventions 2-1100

Methods for distinguishing MLL-PTD-positive AML from other AML subtypes and methods for distinguishing specific subtypes against all other subtypes and against each other, the method comprising determining individually the expression level of the markers listed in table 1.1, positions 2-50,and in tables 2-3. Use of said markers for the manufacture of diagnostics. Diagnostic kits containing said markers and apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression levels of said markers.

The application lacks unity within the meaning of Rule 13.1 PCT.
The problem to be solved in the present application is the provision of markers for distinguishing MLL-PTD-positive AML from other AML subtypes.
The single general concept which can be identified a priori as linking the various inventions and which forms a solution to the above problem relates to the use of "markers for leukemia subtypes". The use of marker genes/nucleotides disclosed in tables 1-3 form 1100 different solutions to the above problem.
However, the concept of using marker genes for distinguishing different leukemia subtypes is know in the art.

The document Schnittger et al. (2002) Blood, Vol. 100(11), Abstract No. 1202 (D1) discloses differentiation of tMLL from MLL_PTD using HOXB5 as a markers. Said marker is described for the same purpose in table 3.9, position 37 of the present application.

The document Schoch et al., PNAS (2002) Vol. 99(15), pp. 10008-10013 (D2), describes a method for distinguishing several forms of AML based on their gene expression profile as determined by using an Affymetrix GeneChip. Class prediction is performed using weighted voting. In tables 1 and 2, sets of genes are disclosed which are sufficient to distinguish between different leukemia subtypes.
KRT18 and CTSW of table 1 of D2 which are used to differentiate t(15;17) vs. t(8;21) are described for the same purpose in table 3.13, position 9 and 1, respectively, of the present application.

CLECSF2, CDW52 and S100A9 are described as distinguishing t(15;17) vs. the rest and are described for the same purpose in table 2.4, positions 5, 25 and 36, respectively.

The document WO-A-03/039433 (D3) describes novel genetic markers for leukemias, identified using differential gene expression analysis on Affymetrix GeneChips. On page 69, line 22 - page 71, line 8, in particular page 70, lines 29-32, the markers ARHGAP4 and CTSW are disclosed for discriminating AML_t(15;17) vs. the rest. Said markers are included in table 2.4, positions 2 and 4, respectively, of the present application for the same purpose.
In addition, the figures of D3, starting from figure 24, list numerous examples of markers for distinguishing leukemia subtypes from each other.

Haferlach et al. (2002) Blood, Vol. 100(11) Abstract No. 731 (D4) disclose a method based on gene expression analysis on microarrays for the identification of signature genes, which enable separation of, e.g., M4eo from al other subtypes with 100% accuracy.

Neben et al. (2002) Blood, Vol. 100(11) Abstract No. 2172 (D5) disclose a method based on gene expression analysis on microarrays for the identification of signature genes, which enable separation of, e.g., MLL-PTD positive patients from MLL-PTD negative patients.

In the light of D1-D5, each document taken alone, the above identified single general concept is not novel and inventive and thus cannot be the single general inventive concept as required by Rule 13.1 PCT.
The present invention is thus considered not the fulfil the requirements of unity as laid down in Rule 13.1 PCT.

No other technical features could be identified that form a technical relationship among each of the separate inventions claimed and which could be considered as same or corresponding special technical features within the meaning of Rule 13.2 PCT.

The first invention was searched, namely methods relaing to distinguishing MLL-PTD-positive AML from other AML subtypes using AAK1 as a marker; kits and apparatus for distinguishing AML-PTD-positive AML from other subtypes using said marker.

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/EP2004/012464

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), SCHNITTGER SUSANNE ET AL: "Acute Myeloid Leukemia (AML) with Partial Tandem Duplication of the MLL-Gene (MLL-PTD) Can Be Discriminated from MLL-Translocations Based on Specific Gene Expression Profiles." XP002270207 Database accession no. PREV200300335802 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 1202, 44th Annual Meeting of the American Society of Hematology;Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971 --- -/--	1-27

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SCHOCH CLAUDIA ET AL: "Acute myeloid leukemias with reciprocal rearrangements can be distinguished by specific gene expression profiles" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 99, no. 15, 23 July 2002 (2002-07-23), pages 10008-10013, XP002215484 ISSN: 0027-8424 the whole document in particular tables 1 and 2	1-27
Y	WO 03/039443 A (DEUTSCHES KREBSFORSCH ;HAFERLACH TORSTEN (DE); EILS ROLAND (DE); K) 15 May 2003 (2003-05-15) the whole document in particular Examples 4, 6 and 7	1-27
Y	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), HAFERLACH TORSTEN ET AL: "Gene Expression Profiling Is Able To Reproduce Different Phenotypes in AML as Defined by the FAB Classification." XP002269981 Database accession no. PREV200300357598 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 731, 44th Annual Meeting of the American Society of Hematology;Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971	1-27
Y	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), NEBEN KAI ET AL: "Acute Myeloid Leukemia with Normal Karyotype and Mutation of the FLT3 or MLL Gene Are Characterized by Specific Gene Expression Profiles." XP002270208 Database accession no. PREV200300336869 abstract -/--	1-27

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	& BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 2172, 44th Annual Meeting of the American Society of Hematology;Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971	
Y	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2001 (2001-11-16), SCHNITTGER SUSANNE ET AL: "Partial tandem duplications (PTD) of the MLL gene: A study of 1603 patients reveals high frequency in secondary acute myeloid leukemia and low association with trisomy 11" XP002270209 Database accession no. PREV200200261466 abstract & BLOOD, vol. 98, no. 11 Part 1, 16 November 2001 (2001-11-16), page 801a, 43rd Annual Meeting of the American Society of Hematology, Part 1;Orlando, Florida, USA; December 07-11, 2001 ISSN: 0006-4971	1-27
Y	KOHLMANN A ET AL: "MOLECULAR CHARACTERIZATION OF ACUTE LEUKEMIAS BY USE OF MICROARRAY TECHNOLOGY" GENES, CHROMOSOMES & CANCER, XX, XX, vol. 37, no. 4, August 2003 (2003-08), pages 396-405, XP008025253 the whole document in particular table 2	1-27
Y	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2001 (2001-11-16), SCHOCH CLAUDIA ET AL: "Specific abnormalities on the genomic level result in a distinct gene expression pattern detected by oligonucleotide microarrays: An analysis of 25 patients with AML M2/t(8;21), AML M3/M3v/t(15;17), and AML M4eo/inv(16)" XP002269491 Database accession no. PREV200200129822 abstract -/--	1-27

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	& BLOOD, vol. 98, no. 11 Part 1, 16 November 2001 (2001-11-16), pages 92a-93a, 43rd Annual Meeting of the American Society of Hematology, Part 1;Orlando, Florida, USA; December 07-11, 2001 ISSN: 0006-4971	
Y	EP 1 043 676 A (WHITEHEAD BIOMEDICAL INST) 11 October 2000 (2000-10-11) the whole document	1-27
Y	GOLUB T R ET AL: "Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 286, no. 5439, 15 October 1999 (1999-10-15), pages 531-537, XP002207658 ISSN: 0036-8075 cited in the application the whole document	1-27
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Patent Family Annex

Information on patent family members

International Application No
PCT/EP2004/012464

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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Important Information

general

- the **claims cannot be changed** at this point in the procedure, the transmitted report is **not** the ISR (see PCT Art. 19)
- non-payment does not lead to a **loss of rights**, a new procedure will be started on entry into the regional or national phase
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- no **protest fee** needs to be paid yet, only additional **search fee(s)**